REMARKS

Claims 2-7, 11-14, 28-34, 37, 38, 46, 49-51, 53-65, 67, 68, 72, 74-78, 92-96, 100 and 101 are pending. Claims 1, 8-10, 15-27, 35, 36, 39-45, 47, 48, 52, 66, 69-71, 73, 79-91 and 97-99 are canceled. Applicants request entry of amendments to claims 2-7, 11-14, 28-31, 34, 46, 63-65, 67, 68 and 92-94. As originally filed the claim after claim 47 and before claim 49 was misnumbered as claim 44. This claim is currently shown in the listing of claims above as being canceled claim 48. The basis for the amendments can be found throughout the specification especially in the examples. Claims 1 is canceled and has been rewritten as new claim 102. Claim 102 more clearly defines that which is being claimed in the instant application. Claim 103 has also been newly added and is supported in the specification particularly in the examples at for example starting at page 92, Example 2.

Rejection Under 35 U.S.C. §103(a)

Claims 1-101 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Elbashir *et al.*, The EMBO Journal, 2001, Vol. 20, No. 23, pages 6877-6888 (the Elbashir reference); Fosnaugh *et al.*, US 2003/0143732 (the Fosnaugh reference); and Morrissey *et al.*, US 2003/0206887 (the Morrissey reference). Claims 1, 8-10, 15-27, 35, 36, 39-45, 47, 48, 52, 66, 69-71, 73, 79-91 and 97-99 have been canceled herein obviating the rejection against these claims. Applicants respectfully traverse the rejection for the following reasons.

The Office has characterized the instant claims as being drawn to methods of inhibiting gene expression in a tissue or an animal comprising administration of compositions comprising siRNA oligonucleotides comprising various motifs. The Office Action appears to assert that the instantly claimed oligomeric compounds and compositions would be obvious in view of the cited references disclosing methods of using modified compositions having modified nucleosides that are common with those being claimed. Applicants disagree with this characterization as the present claims are drawn to oligomeric compounds, compositions and methods of using them and are not limited to methods. Furthermore, Applicant's compositions and oligomeric compounds have unique motifs not shown or suggested in the cited references.

Applicants submit that the office action has not established a *prima facie* case of obviousness. To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

Both the Fosnaugh reference and the Morrissey reference were published in 2003 and as such are not available as prior art against the claimed invention which has a priority date of November 5, 2002.

The Elbashir reference discloses siRNA duplexes having 2'-OCH_3 modified nucleosides or deoxyribonucleosides in one or both strands and also discloses that substitution at the 3'-end with 2 or 4 deoxynucleosides. Duplexes in which one or both strands were fully modified with 2'-OCH_3 or 2'-H modified nucleosides negated activity compared to the unmodified duplex. Replacement of the two or four nucleosides at the 3'-ends with 2-deoxyribonucleosides didn't significantly alter the activity relative to the unmodified duplex. The reference concluded that extensive modification with 2'-OCH_3 or 2'-deoxy ribonucleosides reduce the ability of the duplex to mediate RNAi. The reference therefore, teaches away from extensive modification with deoxynucleosides except at the 3'-end. Furthermore, the reference does not teach or suggest motifs comprising alternating 2'-deoxy and 2'-modified nucleosides as taught in the instant application.

In conclusion, the currently outstanding rejection under 103 is improper because: a) the Fosnaugh and Morrissey references are not available as prior art; b) the Elbashir reference does not teach or suggest all the limitations; and c) the Elbashir reference teaches away from the extensively modified duplexes claimed in the instant application. Applicants therefore respectfully request reconsideration and withdrawal of the rejection.

It is believed all of the claims presently before the Office patentably define the invention over the prior art and are otherwise in condition for ready allowance. An early Office Action to that effect is, therefore, earnestly solicited.

Respectfully submitted,

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